

REMARKS

With this Amendment, claims 21, 23-29, and 31-37 are pending in this application. Claims 1-20, 22, and 30 are cancelled without prejudice. To more clearly define the subject matter of the invention, Applicants request entry of amendments to claims 21, 25-28, and 31 and addition of claims 32-37.

The claims, as amended, encompass methods of administering CD105+ cells. Support for the amendments can be found throughout the specification, including e.g., in Example 10, which recites induction of chondrogenic differentiation by "CD105+ cells" in alginate culture (page 30, line 10 to page 31, line 2). Support for the use of both expanded and non-expanded CD105+ cells in the claimed methods can be found at, e.g., at page 28, line 20 to page 29, line 10, reciting tissue culture expanded CD105+ cells and at, e.g., page 6, lines 11-14, reciting non-tissue culture expanded CD105+ cells.

The amended claims are not limited to purified cells isolated from bone marrow by a specific process. These amended claims are supported by both the specification and original claims 15, 21, and 26-28. New claims 32-34 and 35-37 depend on claims 26 and 27, respectively, and mirror claims 23-25. Claims 25, 28, and 31 have been amended to correct grammatical formalities.

No new matter has been added by this Amendment. Applicants respectfully request entry and favorable consideration of the amended claims.

REJECTIONS UNDER 35 U.S.C. § 103

The Examiner rejected claims 21 and 23-31 under 35 U.S.C. § 103(a) as allegedly obvious over WO/29552 in view of U.S. Patent No. 6,287,816 ("the '816 patent"). Applicants respectfully submit that this rejection should be withdrawn for the reasons argued previously in prosecution of this application. However, in an effort to expedite prosecution, Applicants provide a Declaration Under 37 C.F.R. § 1.131 executed by Dr. Manas Majumdar ("the Majumdar Declaration"). Dr. Majumdar, a named inventor, demonstrates that the claimed invention was reduced to practice prior to May 25, 2000, the publication date of WO 00/29552. Applicants note that the submission of this Declaration should not be construed as an admission that the pending claims are obvious over WO 00/29552 in view of the '816 patent.

To comply with 37 C.F.R. § 1.131, an "affidavit or declaration must establish possession of the whole invention claimed or something falling within the claim (such as a species of a genus claim), in the sense that the claim as a whole reads on it. . . . Even if applicant's 37 C.F.R. § 1.131 affidavit is not fully commensurate with the rejected claim, the applicant can still overcome the rejection by showing that the differences between the claimed invention and the showing under 37 C.F.R. § 1.131 would have been obvious to one of ordinary skill in the art, in view of applicant's 37 C.F.R. § 1.131 evidence, prior to the effective date of the reference(s) or the activity." M.P.E.P. § 715.02, citing *In re Tanczyn*, 342 F.2d 830, 146 U.S.P.Q. 298 (C.C.P.A. 1965) and *In re Spiller*, 500 F.2d 1170, 182 U.S.P.Q. 614 (C.C.P.A. 1974).

Applicants submit that the Majumdar Declaration demonstrates that the methods of at least claims 21 and 23-25 were reduced to practice before May 25, 2000 and that claims 26-29, 31, and new claims 32-37 would have been obvious to one of skill in the art in view of this evidence.

Amended claim 21 recites (emphasis added):

21. A method for inducing chondrogenesis, said method comprising administering an effective amount of a composition comprising CD105+ cells isolated from bone marrow and a suitable matrix carrier.

The Majumdar Declaration and the accompanying Exhibits demonstrate reduction to practice of each essential element of claim 21 prior to May 25, 2000. Exhibits A and D show "CD105+ cells isolated from bone marrow" by two distinct processes (Majumdar Dec. at ¶¶ 5 and 8). Exhibit B shows a "composition" comprising these cells and "a suitable matrix carrier," e.g., alginate (Majumdar Dec. at ¶ 6). Exhibits C and E show "a method for inducing chondrogenesis," confirmed by detection of a chondrogenic marker in CD105+ cells in alginate culture (Majumdar Dec. at ¶¶ 7 and 9).

Amended claims 23-25 recite:

- 23. The method of claim 21 further comprising administering a bone and or cartilage inducing factor.
- 24. The method of claim 23 wherein said factor is a BMP.
- 25. The method of claim 24 wherein the BMP is BMP-2 or BMP-9.

The Majumdar Declaration also demonstrates reduction to practice of these methods before May 25, 2000. For example, Exhibit C shows induction of chondrogenesis upon treatment of CD105+ cells with BMP-2 (Majumdar Dec. at ¶ 7), and Exhibit E shows induction of chondrogenesis upon treatment of CD105+ cells with BMP-2 or BMP-9 (Majumdar Dec. at ¶ 9). Accordingly, Applicants submit that the Majumdar Declaration establishes possession, by actual reduction to practice, of at least claims 21 and 23-25 before May 25, 2000.

Applicants' prior reduction to practice of the methods of at least claims 21 and 23 is also demonstrated by Exhibit F, a true and accurate copy of Majumdar et al., J. Cell Physiol. 185: 98-106 (2000). This article describes isolation of CD105+ cells from bone marrow, culture in alginate, and induction of chondrogenesis upon treatment of alginate-cultured CD105+ cells with TGF- β . As noted in the lower right corner of the first page of Exhibit F, this paper was received by the publisher on February 2, 2000 and accepted for publication on April 13, 2000. Exhibit F thus provides further external corroboration of Applicant's possession of the method of at least claims 21 and 23 prior to May 25, 2000.

Without comment as to reduction to practice of the methods of claims 26-29 and 31-37 prior to May 25, 2000, Applicants submit that these methods would have been obvious to one of ordinary skill in the art, in view of Applicants' 37 C.F.R. § 1.131 evidence. These claims relate to therapeutic applications of the methods of claims 21 and 23-25. The potential for therapeutic use of mesenchymal stem cells (MSCs) was

well known in the art prior to May 25, 2000. As noted in 1999 by Barry et al. (cited by the Examiner), MSCs “present exciting opportunities for cell-based therapeutic applications” and “therapeutic modalities have been described for use of MSCs in cartilage . . . regeneration” (page 134, left column). However, Barry notes in the same paragraph that “these cells have a multipotent capacity and can differentiate along a number of well characterized cell lineages” (page 134, left column). Thus, one of ordinary skill in the art would have known how to practice cartilage-related therapeutic applications with MSCs if shown how to induce an isolated MSC population to differentiate down the chondrogenic lineage. In view of Applicants’ disclosure of methods for isolating a population of MSCs based on expression of CD105 and methods for inducing chondrogenic differentiation of these cells, the skilled artisan would have considered the therapeutic methods of claims 26-29 and 31-37 to be obvious on their face, including methods for treating arthritis (claim 26 and 32-34), methods for treating articular cartilage defects or damage (claim 27 and 35-37), and methods for repairing cartilage tissue (claims 28, 29, and 31).

The Majumdar Declaration thus shows that Applicants possessed the methods of claims 26-29 and 31-37, in addition to those of claims 21 and 23-25, since “possession of what is shown carries with it possession of variations and adaptations which would have been obvious, at the time, to one of ordinary skill in the art” M.P.E.P. 715.02, citing *In re Spiller*, 500 F.2d 1170, 182 U.S.P.Q. 614 (C.C.P.A. 1974).

In view of the above, Applicants have established actual reduction to practice of at least claims 21 and 23-25 prior to May 25, 2000. Further, the methods of claims 26-29 and 31-37 would have been obvious in view of Applicants' 37 C.F.R. §1.131 evidence. Accordingly, Applicants possessed "the whole invention claimed" prior to May 25, 2000 and have antedated WO 00/29552. Accordingly, Applicants respectfully request that the rejection of pending claims 21, 23-29, and 31-37 under 35 U.S.C. § 103(a) be withdrawn.

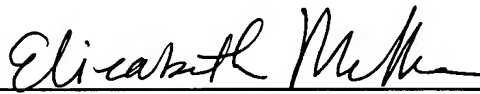
In view of the foregoing remarks, Applicants therefore request the entry of this Amendment, the Examiner's reconsideration and reexamination of the application, and the timely allowance of the pending claims.

Applicants believe that any extension of time required for entry of this Amendment is accounted for by the accompanying Petition for Extension of Time. However, in the event of an error, please grant any additional extensions of time required to enter this response and charge any additional required fees to Deposit Account 06-0916.

Respectfully submitted,

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GARRETT & DUNNER, L.L.P.

Dated: April 5, 2005

By: 
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